

Attorney Docket No: ISIS0038-100/CHEM0001US
Serial No. 10/757,298

May 25, 2006 Response
to September 23, 2005 Action

Listing of the Claims:

1. (*currently amended*) An oligomeric compound comprising a plurality of 2'-hydroxyl ribonucleosides and having a protected phosphate group at the 5'-terminus wherein the protected phosphate group is (S-acetyl-2-thioethyl) phosphate (SATE).

Claims 2 through 5 (*canceled*)

6. (*withdrawn*) An oligomeric compound of claim 1 wherein the protected phosphate group comprises a 7-methylguanosine residue attached to the 5'-position by a triphosphate linkage to give a reverse orientation.

7. (*withdrawn*) An oligomeric compound of claim 6 wherein the 7-methylguanosine residue further comprises an N7 methyl group.

8. (*currently amended*) A double stranded composition comprising an oligomeric compound of claim 1 ~~wherein the oligomeric compound is double stranded.~~

9. (*currently amended*) ~~An oligomeric compound~~ A composition of claim 8 wherein one strand is an antisense strand.

10. (*currently amended*) ~~An oligomeric compound~~ A composition of claim 8 wherein only one strand comprises the protected phosphate group.

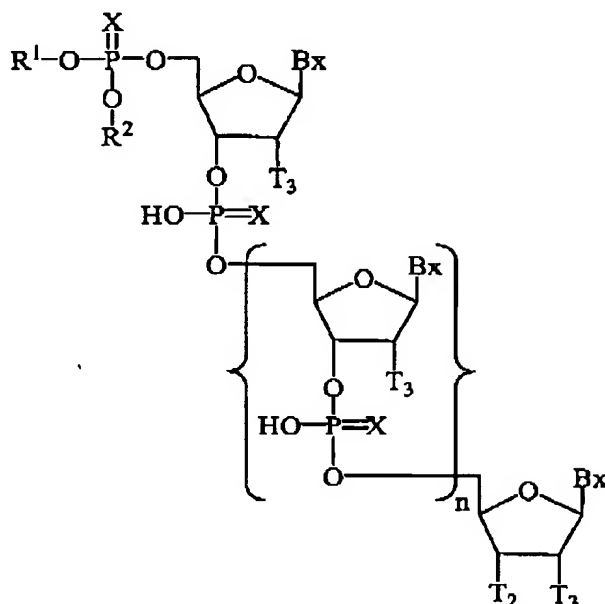
11. (*currently amended*) ~~An oligomeric compound~~ A composition of claim 10 wherein one strand is an antisense strand, and wherein the antisense stand comprises the protected phosphate group.

12. (*currently amended*) ~~An oligomeric compound~~ A composition of claim 8 wherein both strands comprise a protected phosphate group.

13. (*currently amended*) An oligomeric compound of claim 1 having the structure:

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wherein:

T_2 is a hydroxyl group, a protected hydroxyl group, a sugar substituent group, a conjugate group, a nucleoside, a nucleotide, an oligonucleoside, or an oligonucleotide;

each T_3 is, independently, a hydroxyl group, a protected hydroxyl group, a sugar substituent group, a conjugate group, a nucleoside, a nucleotide, an oligonucleoside, or an oligonucleotide;

each X is O or S;

each Bx is an optionally protected heterocyclic base moiety;

n is from 1 to about 50; and

R^1 is H or a phosphorus protecting group and R^2 is a ~~phosphorus protecting group or~~
 ~~R^1 and R^2 are joined in a S-acetyl-2-thioethyl~~ phosphorus protecting group.

14. (previously presented) An oligomeric compound of claim 13 wherein at least one T_3 is F.

15. (currently amended) An oligomeric compound of claim 14 wherein at least one T_3 is F and at least one T_3 is a different sugar substituent group.

Claims 16 through 19 (canceled)

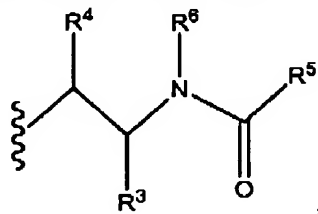
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20. (*withdrawn*) An oligomeric compound of claim 18 wherein R^2 is straight or branched C_1 - C_{12} alkyl or cyano C_1 - C_{12} alkyl.

21. (*withdrawn*) An oligomeric compound of claim 18 wherein R^2 is cyanoethyl.

22. (*withdrawn*) An oligomeric compound of claim 18 wherein R^2 is a group of formula:



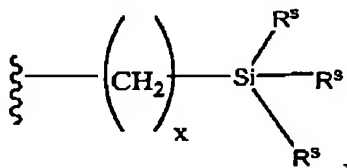
wherein:

R^5 is substituted or unsubstituted alkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, or substituted or unsubstituted heterocycloalkyl;

R^6 is R^5 or H; and

each of R^3 and R^4 is R^6 , or together form a cycloalkyl ring or a heterocycloalkyl ring, each of which is optionally substituted.

23. (*withdrawn*) An oligomeric compound of claim 18 wherein R^2 is a group of formula:



wherein:

each R^s is, independently, alkyl or aryl; and

x is an integer from 1 to about 12.

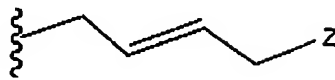
24. (*withdrawn*) An oligomeric compound of claim 23 wherein x is from 1 to about 8.

25. (*withdrawn*) An oligomeric compound of claim 24 wherein x is from 1 to 3.

26. (*withdrawn*) An oligomeric compound of claim 18 wherein R^2 is a group of formula:

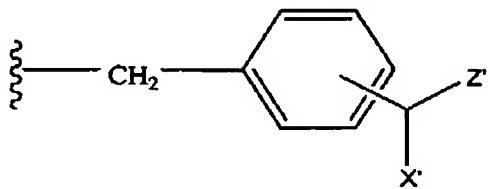
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wherein Z is CN, halogen, NO₂, alkaryl, sulfoxy, sulfonyl, thio, substituted sulfoxy, substituted sulfonyl, or substituted thio.

27. (*withdrawn*) An oligomeric compound of claim 18 wherein R² is a group of formula:

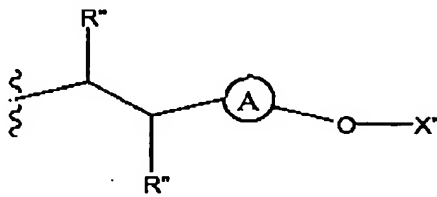


wherein:

Z' is CN, halogen, substituted sulfoxy, substituted sulfonyl, or a substituted thio group; and

X' is Z' or H.

28. (*withdrawn*) An oligomeric compound of claim 18 wherein R² is a group of formula:



wherein:

A is a diradical of a mono- or bi-cyclic aromatic ring system;

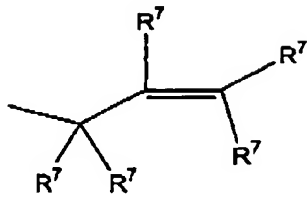
X'' is alkaryl, aralkyl, sulfonyl, thio, substituted sulfonyl, substituted thio, or (CO)-R^x, wherein R^x is a substituent or -(CH₂-CH₂)₀₋₁-Si(R^{Si})₃, wherein each R^{Si} is, independently, an alkyl moiety; and

each R'' is, independently, H, alkyl, aryl, heteroalkyl, heteroaryl, alkyaryl, or aralkyl or two R'' groups together with the carbon atoms to which they are attached form an optionally substituted aliphatic or aromatic ring system.

29. (*withdrawn*) An oligomeric compound of claim 18 wherein R² is a group of formula:

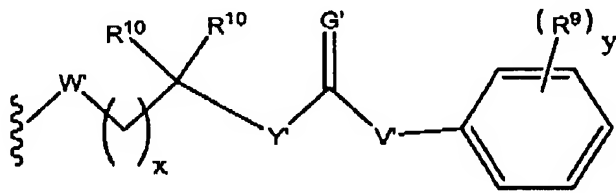
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wherein each R^7 is, independently, H, alkyl, alkenyl, alkynyl, or aryl.

30. (*withdrawn*) An oligomeric compound of claim 18 wherein R^2 is a group of formula:



wherein:

each R^{10} is, independently, H, alkyl, alkenyl, alkynyl, or aryl;

W' and G' are each, independently, O or S;

Y' is, independently, O or NR^8 , wherein R^8 is H, alkyl, alkenyl, alkynyl, cycloalkyl, or phenyl;

V' is, independently, a single bond, O or NR^8 ;

R^9 is alkyl, alkenyl, alkynyl, cycloalkyl, CN, NO_2 , Cl, Br, I, CF_3 , OR^8 , NR^8R^8 , or phenyl;

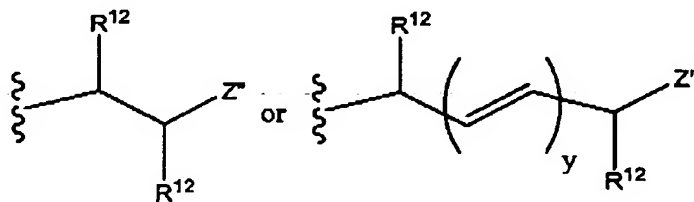
y is 0, 1, 2 or 3; and

x is an integer from 1 to about 12.

31. (*withdrawn*) An oligomeric compound of claim 30 wherein x is from 1 to about 8.

32. (*withdrawn*) An oligomeric compound of claim 30 wherein x is from 1 to 3.

33. (*withdrawn*) An oligomeric compound of claim 18 wherein R^2 is a group of formula:



wherein:

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Z" is an electron withdrawing group; and

each R¹² is H, substituted or unsubstituted alkyl, substituted or unsubstituted heterocycloalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, or substituted or unsubstituted heterocycloalkyl.

34. (*withdrawn*) A method of reducing the expression of a nucleic acid molecule encoding a target comprising contacting the nucleic acid molecule with a compound of claim 1, wherein the compound hybridizes with the nucleic acid molecule encoding the target and reduces the expression of the target.

35. (*withdrawn*) A method of screening for a modulator of a target comprising:
contacting a suitable target segment of a nucleic acid molecule encoding the target with one or more candidate modulators of the target; and
identifying one or more modulators of the target expression which modulate the expression of the target.

36. (*withdrawn*) A method of claim 35 wherein the modulator of the target expression comprises an oligonucleotide, an antisense oligonucleotide, a DNA oligonucleotide, an RNA oligonucleotide, an RNA oligonucleotide having at least a portion of the RNA oligonucleotide capable of hybridizing with RNA to form an oligonucleotide-RNA duplex, or a chimeric oligonucleotide.

37. (*withdrawn*) A diagnostic method for identifying a disease state comprising identifying the presence of a target in a sample using at least one primer designed to the target, wherein the primer is a compound of claim 1, and wherein the presence of the target indicates the presence of the disease state.

38. (*previously presented*) A kit or assay device comprising a compound of claim 1.

39. (*withdrawn*) A method of treating an animal having a disease or condition associated with a target comprising contacting the animal with a therapeutically or prophylactically effective amount of a compound of claim 1 so that expression of the target is reduced.

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40. (*withdrawn*) A method of reducing the expression of a gene in a biological system expressing the gene comprising contacting the biological system with a composition comprising a compound of claim 1 under conditions effective to reduce the expression of the gene, wherein the compound comprises at least one RNA strand having at least one modified nucleoside, wherein the modified nucleoside has a phosphate precursor moiety..

41. (new) A double stranded composition comprising an oligomeric compound of claim 13.